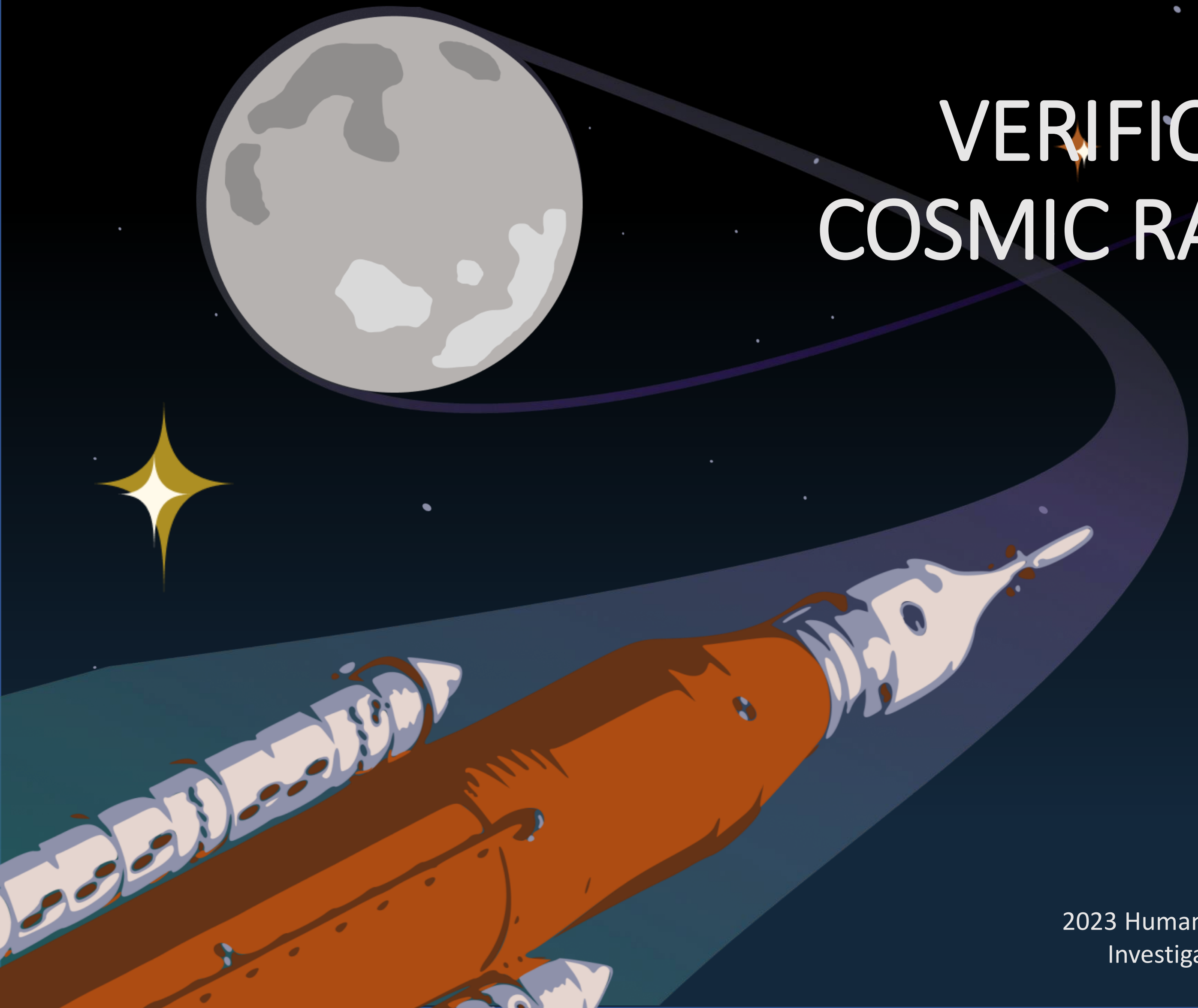

VERIFICATON OF NASA GALACTIC COSMIC RAY SIMULATOR FOR LARGE ANIMAL MODELS

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Outline

- Galactic Cosmic Ray Simulator (GCRsim) Beam Overview
- Transport Studies
- Digital Phantoms
- Simulation Results of GCRsim Beam in the Three Different Phantoms
- Summary and Conclusions

GCRsim Beam Overview: Background

- Space radiation poses multiple important health risks for astronauts
  - Cancer
  - Cardiovascular disease
  - Damage to Central Nervous System
- For long duration mission beyond low Earth orbit (LEO) risks mainly arise from galactic cosmic rays (GCR)
- Ground-based experiments will help to mitigate risks and reduce uncertainties

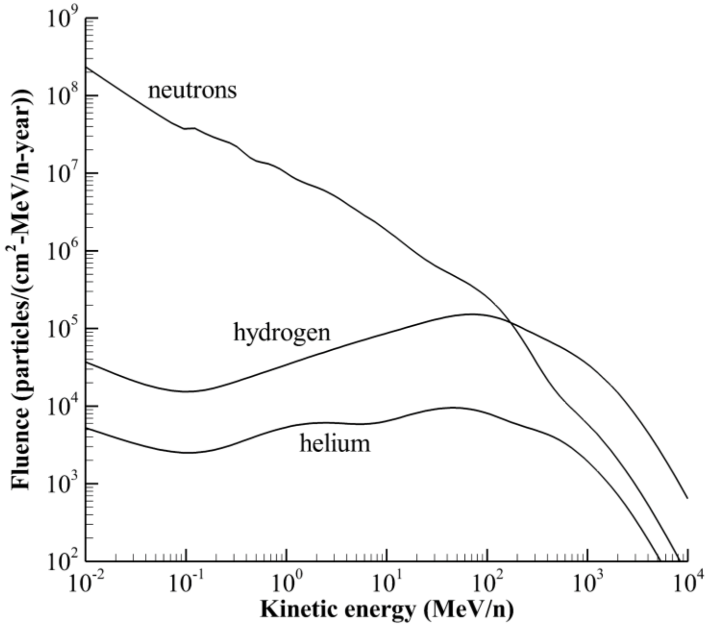
GCRsim Beam Overview: Objective

- Previous ground-based radiation studies mainly utilized single mono-energetic beams
  - Collectively improved our understanding of underlying biological mechanism
  - Poor analog for the complete space environment
- The GCR simulator (GCRsim) was developed at the NASA Space Radiation Laboratory (NSRL) to better represent the complex mixed field environment in space
- GCRsim is intended simulate radiation environment as seen by astronauts in deep space
  - Study health effects of GCR
  - Improve risk projections
  - Countermeasure development and testing

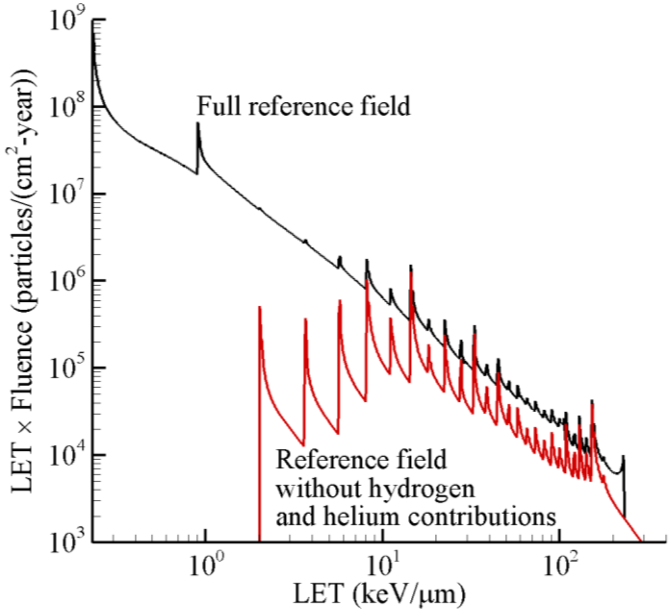
NASA's NSRL facility in Brookhaven, NY

GCRsim Beam Overview: Reference Field

- A single reference field was defined to approximate deep space environment
  - Female BFO (blood forming organ) behind 20 g/cm^2 spherical aluminum shielding during solar minimum



Reference field energy spectra for neutrons, hydrogen, and helium [Slaba et al. 2016]



Differential LET spectra of reference field with and without contributions from hydrogen and helium [Slaba et al. 2016]

GCRsim Beam Overview: Beam Definition

- The GCRsim at NSRL is designed to deliver deep space, shielded tissue environment to biological targets in a laboratory setting
- 33 mono-energetic beams of varying energies with ion species consisting of H, He, C, O, Fe, Si and Ti
- Sequential beam delivery reproducing the space environment over the full range of LET

Ion	Energy (MeV/n)	Range (cm)	LET (keV/µm)	Dose (mGy)
^{1}H	100	*Polyethylene degrader to*		
^{1}H	150	15.9	0.54	35.0
^{1}H	250	38.1	0.39	68.9
^{1}H	1000	326.6	0.22	123.6
^{4}He	100	*Polyethylene degrader to*		
^{4}He	150	16.0	2.17	7.5
^{4}He	250	38.3	1.56	16.4
^{4}He	1000	327.8	0.88	24.9
^{12}C	1000	110.1	7.95	11.7
^{16}O	350	17.0	20.8	15.4
^{28}Si	600	22.7	50.2	8.1
^{48}Ti	1000	32.5	109.5	4.5
^{56}Fe	600	13.1	175.1	4.1
Total				***500.0***

GCRsim beam definition at NASA [Simonsen et al. 2020]

Ion	Energy (MeV/n)	Range (cm)	LET (keV/µm)	Dose (mGy)
^{1}H	20.0	0.43	2.59	30.4
^{1}H	23.3	0.56	2.29	6.7
^{1}H	27.2	0.75	2.02	7.4
^{1}H	31.7	0.98	1.79	8.0
^{1}H	37.0	1.30	1.58	8.7
^{1}H	43.2	1.72	1.39	9.3
^{1}H	50.3	2.26	1.23	10.0
^{1}H	58.7	2.99	1.09	10.6
^{1}H	68.5	3.95	0.97	11.1
^{1}H	79.9	5.20	0.86	11.2
^{1}H	100.0	7.76	0.73	**27.2**

Ion	Energy (MeV/n)	Range (cm)	LET (keV/µm)	Dose (mGy)
^{4}He	20.0	0.43	10.34	**11.0**
^{4}He	23.3	0.57	9.14	**2.1**
^{4}He	27.2	0.75	8.06	**2.2**
^{4}He	31.7	0.99	7.12	**2.3**
^{4}He	37.0	1.31	6.29	**2.5**
^{4}He	43.2	1.73	5.56	**2.6**
^{4}He	50.3	2.28	4.92	**2.7**
^{4}He	58.7	3.01	4.36	**2.7**
^{4}He	68.5	3.97	3.86	**2.7**
^{4}He	79.9	5.23	3.43	**2.7**
^{4}He	100.0	7.81	2.90	**6.1**

Transport Studies

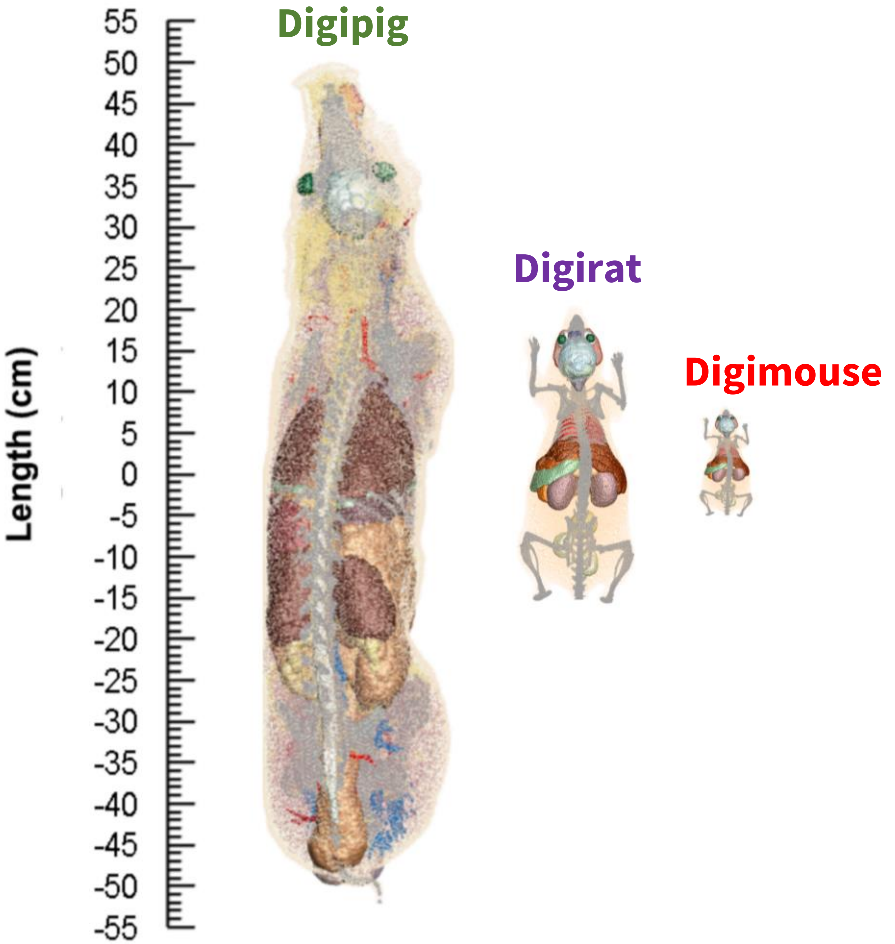
- The GCRsim is suitable for animal models such as mice and rats to represent internal radiation environment seen at critical organ locations within the human body

- Radiation transport studies using phantom models of mouse (Digimouse) and rat (Digirat) have been previously completed [Simonsen et al. 2020]
  - Geant4 Monte Carlo code was used to simulate the GCRsim in the digital phantoms

- Verified key physical parameters of the GCRsim beams
  - Homogeneous internal dose distribution across radiosensitive tissues
  - Reproduces the dose and fluence spectra of the reference field as function of linear transfer energy (LET)

Digital Phantoms

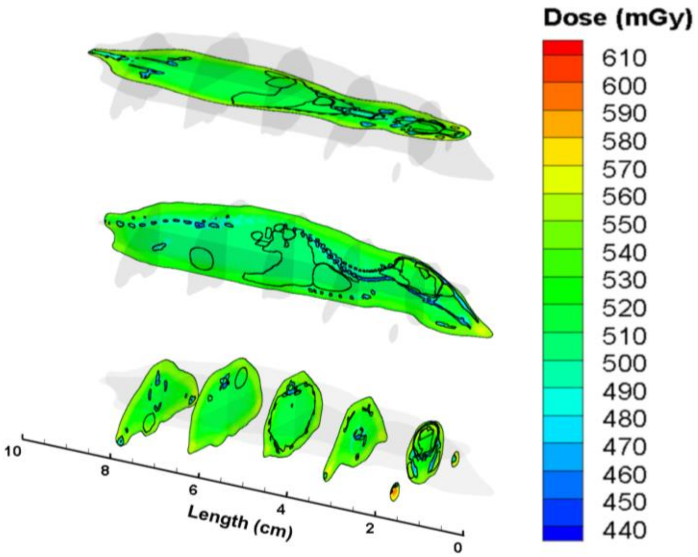
- Digital phantoms are voxelized 3D models of an animal created from CT or MR images
  - Digimouse: Digital model of 28 g male mouse
  - Digirat: scaled model of Digimouse resulting in a 754 g rat
  - Digipig: Digital model of a 35 kg male minipig
- Each voxel identifies important radiosensitive tissues
  - Quantities of interest were calculated in these radiosensitive organs
- Simulations performed with each of these phantoms
  - Geant4 Monte Carlo simulation
  - 500 mGy GCRsim beam dose
  - Isotropic irradiation conditions



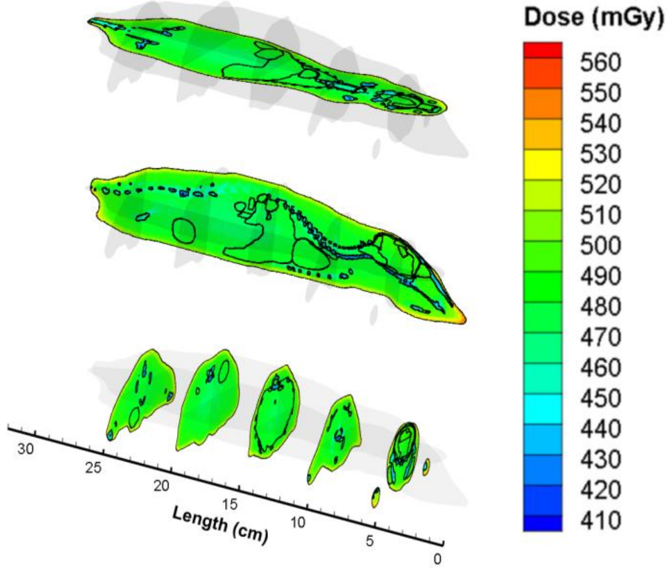
Digipig, Digirat and Digimouse shown side by side for comparison

Simulation Results: Dose Distribution

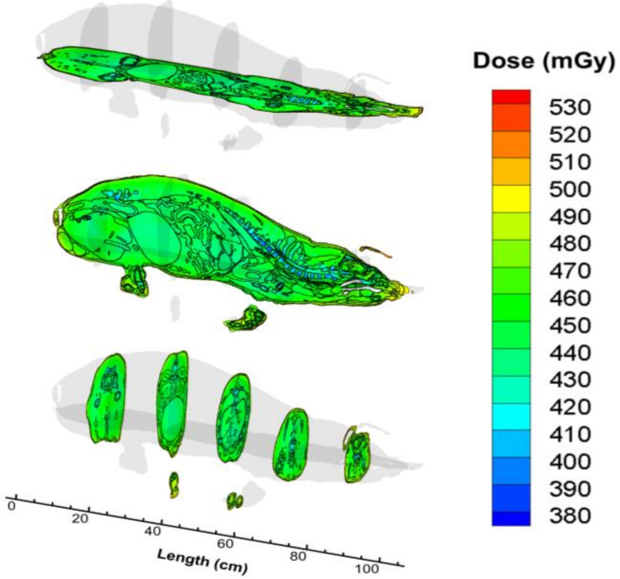
Digimouse
Mean voxel dose: 515 mGy



Digirat
Mean voxel dose : 489 mGy



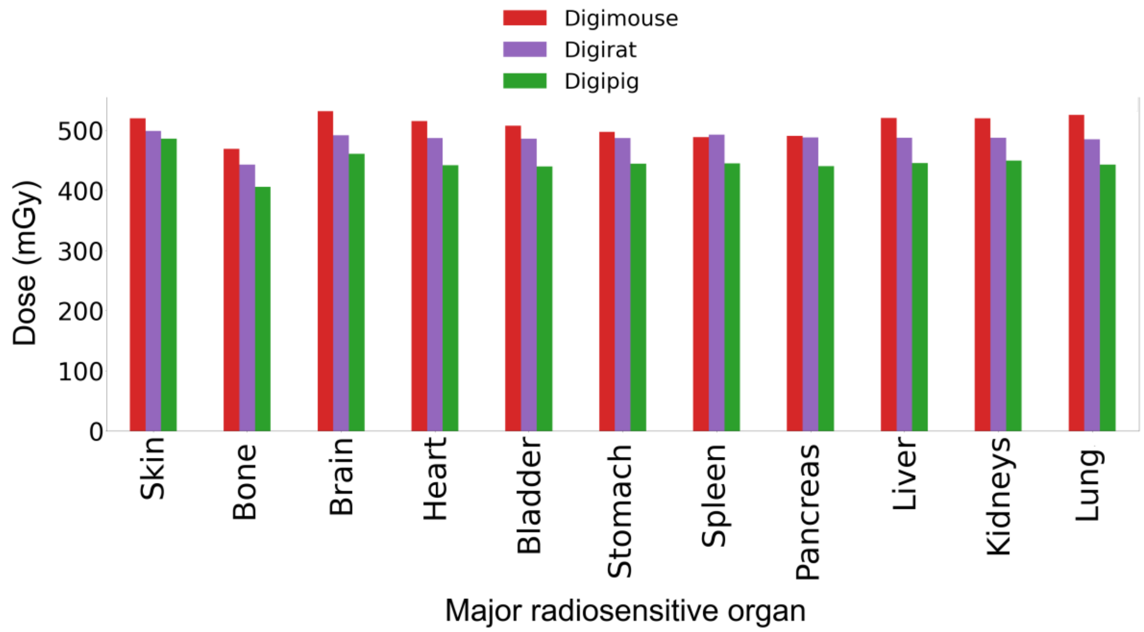
Digipig
Mean voxel dose: 451 mGy



- Relatively homogonous dose distribution was seen throughout all three animal phantoms
- 95% of the voxel doses were within 6%, 7%, and 8% of the mean values in Digimouse, Digirat, and Digipig, respectively

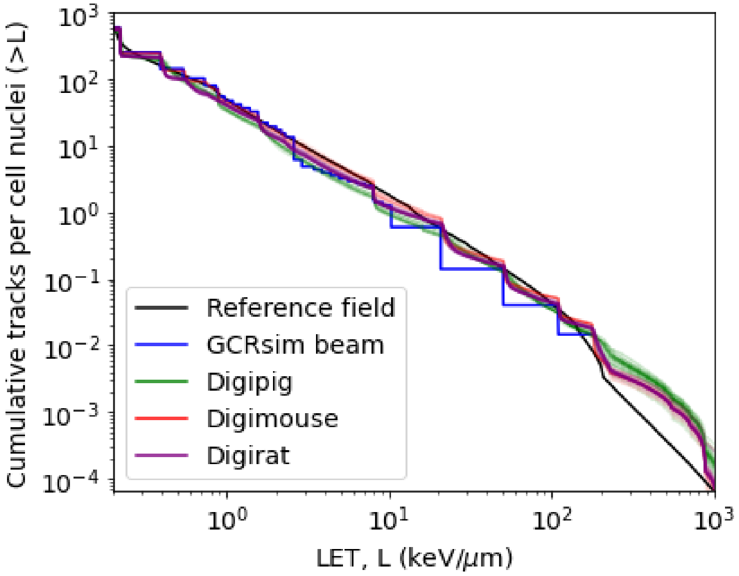
Simulation Result: Tissue Dose

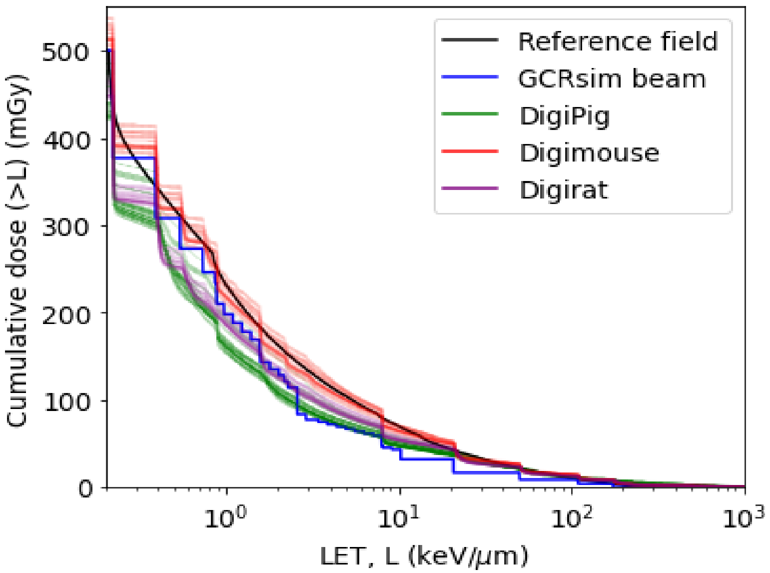
- No major variation in tissue doses was observed
  - All values compared well with beam dose of 500 mGy
  - Bone dose slightly lower in all animals due to density difference
- Digimouse: mean soft tissue dose was 4.6% higher than the beam dose
  - Bone dose was 6% lower
- Digirat: mean soft tissue dose 2% lower than the beam dose
  - Bone dose was 11% lower
- Digipig: mean soft tissue dose about 10% lower than the beam dose
  - Bone dose was 20% lower



Side by side comparison of simulated dose in major radiosensitive organs of Digimouse, Digirat and Digipig.

Simulation Result: Fluence and Dose Spectra





Comparison of the cumulative fluence (on the left), and cumulative dose (on the right) as a function of LET within radiosensitive organs of the three different animal phantoms

- Simulated spectra in all three animal models compare well with reference field
- The difference between the phantoms and the reference field was less than 15% in LET domain that contributes most heavily to dose

Summary and Conclusion

- It was shown from the Monte Carlo simulations that the relevant radiation quantities in larger animals such as minipigs have comparable values to rodent models and the reference field.

- The differences observed were within expectations due to the increased mass and most likely not substantial enough to significantly change biological responses.

- These results suggest that no major modifications may be required for the existing GCRsim beam to support studies with large animal models.

- Nevertheless, further analysis with large animals may be needed to evaluate the radiation field in the internal organs for specific experimental design considerations.

Refences

- [Simonsen et al. 2020] Simonsen, L. C., T. C. Slaba, P. Guida, and A. Rusek. "NASA's first ground-based galactic cosmic ray simulator: Enabling a new era in space radiobiology research." PLoS Biology 18, no. 5 (2020): e3000669.

- [Slaba et al. 2016] Slaba, T. C., S. R. Blattnig, J. W. Norbury, A. Rusek, and C. La Tessa. "Reference field specification and preliminary beam selection strategy for accelerator-based GCR simulation." Life Sciences in Space Research 8 (2016): 52-67